



13

1

SEQUENCE LISTING

<110> Crooke, Stanley T  
Lima, Walter  
Wu, Hongjiang

<120> Methods of Using Mammalian RNase H and Compositions Thereof

<130> ISPH-0520

<140> US 09/781,712  
<141> 2001-02-12

<150> US 60/067,458  
<151> 1997-12-04

<150> US 09/203,716  
<151> 1998-12-02

<150> US 09/343,809  
<151> 1999-06-30

<150> US 09/684,254  
<151> 2000-10-06

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<170> PatentIn version 3.1

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35 40 45

Ile Cys Tyr Cys Pro Leu Pro Arg Leu Ala Asp Leu Glu Ala Leu Leu  
50 55 60

Val Ala Asp Ser Leu Thr Leu Leu Glu Ser Glu Arg Glu Arg Leu Phe  
65 70 75 80

Ala Leu Met Glu Asp Thr Asp Phe Val Gly Trp Ala Leu Asp Val Leu  
85 90 95

Ser Pro Asn Leu Ile Ser Thr Ser Met Leu Gly Trp Val Leu Tyr Asn

100	105	110
Leu Asn Ser Leu Ser His Asp Thr Ala Thr Gly Leu Ile Gln Tyr Ala		
115	120	125
Leu Asp Gln Gly Val Asn Val Thr Gln Val Phe Val Asp Thr Val Gly		
130	135	140
Met Pro Glu Thr Tyr Gln Ala Arg Leu Gln Gln Ser Phe Pro Gly Ile		
145	150	155
Glu Val Thr Val Leu Ala Leu Ala Asp Ala Leu Tyr Pro Val Val Ser		
165	170	175
Ala Ala Ser Ile Cys Ala Leu Val Ala Arg Asp Gln Ala Val Leu Leu		
180	185	190
Trp Gln Phe Val Glu Leu Leu Gln Asp Leu Asp Thr Asp Tyr Gly Ser		
195	200	205
Gly Tyr Pro Asn Asp Pro Leu Thr Leu Ala Trp Leu Leu Glu His Val		
210	215	220
Glu Pro Val Phe Gly Phe Pro Gln Phe Val Arg Phe Ser Trp Arg Thr		
225	230	235
Ala Gln Thr Ile Leu Glu Leu Glu Ala Glu Asp Val Ile Trp Glu Asp		
245	250	255
Ser Ala Ser Glu Asn Gln Glu Gly Leu Arg Leu Ile Thr Ser Tyr Phe		
260	265	270
Leu Asn Glu Gly Ser Gln Ala Arg Pro Arg Ser Ser His Arg Tyr Phe		
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Leu Glu Arg Gly Leu Glu Ser Ala Thr Ser Leu		
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Val Asp Glu Ala Gly Arg Gly Pro Val Leu Gly Pro Met Val Tyr Ala  
35 40 45

Ile Cys Tyr Cys Pro Leu Ser Arg Leu Ala Asp Leu Glu Ala Leu Leu  
50 55 60

Val Ala Asp Ser Leu Thr Leu Thr Glu Asn Glu Arg Glu Arg Leu Phe  
65 70 75 80

Ala Leu Met Glu Glu Asp Gly Asp Phe Val Gly Trp Ala Leu Asp Val  
85 90 95

Leu Ser Pro Asn Leu Ile Ser Thr Ser Met Leu Gly Arg Val Leu Tyr  
100 105 110

Asn Leu Asn Ser Leu Ser His Asp Thr Ala Ala Gly Leu Ile Gln Tyr  
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Val Leu Gly Ile Asp Glu Ala Gly Arg Gly Pro Val Leu Gly Pro Met  
35 40 45

Val Tyr Ala Ala Ala Ile Ser Pro Leu Asp Gln Asn Val Glu Leu Leu  
50 55 60

Asn Leu Gly Val Asp Asp Ser Leu Ala Leu Asn Glu Ala Leu Arg Glu  
65 70 75 80

Glu Ile Phe Asn Leu Met Asn Glu Asp Glu Asp Ile Gln Gln Ile Ile  
85 90 95

Ala Tyr Ala Leu Arg Cys Leu Ser Pro Glu Leu Ile Ser Cys Ser Met

100	105	110
Leu Leu Arg Gln Leu Tyr Ser	Leu Asn Glu Val Ser His Glu Ala Ala	
115	120	125
Ile Thr Leu Ile Arg Asp Ala Leu Ala Cys Asn Val Asn Val Val Glu		
130	135	140
Ile Leu Val Asp Thr Val Gly Pro Leu Ala Thr Tyr Gln Ala Leu Leu		
145	150	155 160
Glu Leu Leu Phe Pro Gly Ile Ser Ile Cys Val Thr Glu Leu Ala Asp		
	165	170 175
Ser Leu Phe Pro Ile Val Ser Ala Ala Ser Ile Ala Ala Leu Val Thr		
	180	185 190
Arg Asp Ser Arg Leu Arg Asn Trp Gln Phe Arg Glu Leu Asn Ile Leu		
	195	200 205
Val Pro Asp Ala Gly Tyr Gly Ser Gly Tyr Pro Gly Asp Pro Asn Thr		
	210	215 220
Leu Leu Phe Leu Gln Leu Ser Val Glu Pro Val Phe Gly Phe Cys Ser		
	225	230 235 240
Leu Val Arg Ser Ser Trp Leu Thr Ala Ser Thr Ile Val Glu Leu Arg		
	245	250 255
Cys Val Pro Gly Ser Trp Glu Asp Asp Glu Glu Glu Gly Leu Ser Gln		
	260	265 270
Ser Leu Arg Met Thr Ser Trp Met Val Pro Leu Asn Glu Thr Glu Val		
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Val Pro Leu Arg Asn Met Glu Ile Asn Leu Thr Leu Ile Val Ser Thr		
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Leu Phe Leu		
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Pro	Ile	Ile	Met	Gly	Ile	Asp	Glu	Ala	Gly	Arg	Gly	Pro	Val	Leu	Gly	35	40	45	
Pro	Met	Val	Tyr	Ala	Val	Ala	Tyr	Ser	Thr	Gln	Leu	Tyr	Gln	Asp	Glu	50	55	60	
Thr	Ile	Ile	Pro	Asn	Tyr	Glu	Phe	Asp	Asp	Ser	Leu	Leu	Leu	Thr	Asp	65	70	75	80
Pro	Ile	Arg	Arg	Met	Leu	Phe	Ser	Leu	Ile	Tyr	Gln	Asp	Asn	Glu	Glu	85	90	95	
Leu	Thr	Gln	Ile	Gly	Tyr	Ala	Thr	Thr	Cys	Ile	Thr	Pro	Leu	Asp	Ile	100	105	110	
Ser	Arg	Gly	Met	Ser	Leu	Phe	Pro	Pro	Thr	Arg	Asn	Tyr	Asn	Leu	Asn	115	120	125	
Glu	Gln	Ala	His	Asp	Val	Thr	Met	Ala	Leu	Ile	Asp	Gly	Val	Ile	Leu	130	135	140	
Gln	Asn	Val	Leu	Leu	Ser	His	Val	Tyr	Val	Asp	Thr	Val	Gly	Pro	Pro	145	150	155	160
Ala	Ser	Tyr	Gln	Leu	Leu	Leu	Glu	Gln	Arg	Phe	Pro	Gly	Val	Leu	Phe	165	170	175	
Thr	Val	Ala	Leu	Leu	Ala	Asp	Ser	Leu	Tyr	Cys	Met	Val	Ser	Val	Ala	180	185	190	
Ser	Val	Val	Ala	Leu	Val	Thr	Arg	Asp	Ile	Leu	Val	Glu	Ser	Leu	Leu	195	200	205	
Arg	Asp	Pro	Asp	Glu	Ile	Leu	Gly	Ser	Gly	Tyr	Pro	Ser	Asp	Pro	Leu	210	215	220	
Thr	Val	Ala	Trp	Leu	Leu	Arg	Asn	Gln	Thr	Ser	Leu	Met	Gly	Trp	Pro	225	230	235	240

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Ala Asn Met Val Arg Phe Ser Trp Gln Thr Cys Gln Thr Leu Leu Asp  
245 250 255

Asp Ala Ser Leu Asn Ser Ile Pro Ile Leu Trp Glu Glu Gln Tyr Met  
260 265 270

Asp Ser Arg Leu Asn Ala Ala Gln Leu Thr Leu Gln Leu Gln Leu Gln  
275 280 285

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290 295 300

Trp Tyr Arg  
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Ile Leu Asp Pro Ala Arg Pro Ile Ala Gly Leu Asn Asp Ser Leu Leu  
35 40 45

Leu Ser Glu Leu Arg Arg Leu Ala Leu Tyr Glu Glu Ile Leu Glu Leu  
50 55 60

Ala Leu Ser Trp Ser Leu Gly Arg Ala Glu Pro His Glu Ile Asp Glu  
65 70 75 80

Leu Asn Ile Leu His Ala Thr Met Leu Ala Met Gln Arg Ala Val Ala  
85 90 95

Gly Leu His Ile Ala Pro Glu Tyr Val Leu Ile Asp Gly Asn Arg Cys  
100 105 110

Pro Leu Leu Pro Met Pro Ala Met Ala Val Val Leu Gly Asp Ser Arg  
115 120 125

Val Pro Glu Ile Ser Ala Ala Ser Ile Leu Ala Leu Val Thr Arg Asp  
130 135 140

Ala Glu Met Ala Ala Leu Asp Ile Val Phe Pro Gln Tyr Gly Phe Ala  
145 150 155 160

Gln His Leu Gly Tyr Pro Thr Ala Phe His Leu Glu Leu Leu Ala Glu  
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His Gly Ala Thr Glu His His Arg Arg Ser Phe Gly Pro Val Leu Arg  
180 185 190

Ala Leu Gly Leu Ala Ser  
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<210> 6  
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<212> PRT  
<213> Homo sapiens

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20 25 30

Arg Gly Arg Leu Thr Gly Val Phe Leu Thr Trp Asn Glu Cys Arg Ala  
35 40 45

Gln Val Asp Arg Phe Pro Ala Ala Arg Phe Leu Leu Phe Ala Thr Glu  
50 55 60

Asp Glu Ala Trp Ala Phe Val Arg Leu Ser Ala Ser Pro Glu Val Ser  
65 70 75 80

Glu Gly His Glu Asn Gln His Gly Gln Glu Ser Glu Ala Leu Pro Gly  
85 90 95

Leu Arg Leu Arg Glu Pro Leu Asp Gly Asp Gly His Glu Ser Ala Gln  
100 105 110

Pro Tyr Ala Leu His Met Leu Pro Ser Val Glu Pro Ala Pro Pro Val  
115 120 125

Ser Arg Asp Thr Phe Ser Tyr Met Gly Asp Phe Val Val Val Tyr Thr  
130 135 140

Asp Gly Cys Cys Ser Ser Asn Gly Arg Arg Leu Pro Arg Ala Gly Ile  
145 150 155 160

Gly Val Tyr Trp Gly Pro Gly His Pro Leu Asn Val Gly Ile Arg Leu  
165 170 175

Pro Gly Arg Gln Thr Asn Gln Arg Ala Glu Ile His Ala Ala Cys Leu  
180 185 190

Ala Ile Glu Gln Ala Leu Thr Gln Asn Ile Asn Leu Leu Val Leu Tyr  
195 200 205

Thr Asp Ser Met Phe Thr Ile Asn Gly Ile Thr Asn Trp Val Gln Gly  
210 215 220

Trp Leu Leu Asn Gly Trp Leu Thr Ser Ala Gly Leu Glu Val Ile Asn  
225 230 235 240

Leu Glu Asp Phe Val Ala Leu Glu Arg Leu Thr Gln Gly Met Asp Ile  
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Gln Trp Met His Val Pro Gly His Ser Gly Phe Ile Gly Asn Glu Glu  
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Ala Asp Arg Leu Ala Arg Glu Gly Ala Leu Gln Ser Glu Asp  
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20 25 30

Arg Gly Arg Leu Thr Gly Val Phe Leu Thr Trp Asn Glu Cys Arg Ala  
35 40 45

Gln Val Asp Arg Phe Pro Ala Ala Arg Phe Leu Leu Phe Ala Thr Glu  
50 55 60

Asp Glu Ala Trp Ala Phe Val Arg Leu Ser Ala Ser Pro Glu Val Ser  
65 70 75 80



Glu Gly His Glu Asn Gln His Gly Gln Glu Ser Glu Ala Leu Ala Ser  
85 90 95

Leu Arg Leu Arg Glu Pro Leu Asp Gly Asp Gly His Glu Ser Ala Glu  
100 105 110

Pro Tyr Ala Leu His Met Leu Pro Ser Val Glu Pro Ala Pro Pro Val  
115 120 125

Ser Arg Asp Thr Phe Ser Tyr Met Gly Asp Phe Val Val Val Tyr Thr  
130 135 140

Asp Gly Cys Cys Ser Ser Asn Gly Arg Arg Arg Pro Arg Ala Gly Ile  
145 150 155 160

Gly Val Tyr Trp Gly Pro Gly His Pro Leu Asn Val Gly Ile Arg Leu  
165 170 175

Pro Gly Arg Gln Thr Asn Gln Arg Ala Glu Ile His Ala Ala Cys Leu  
180 185 190

Ala Ile Glu Gln Ala Leu Thr Gln Asn Ile Asn Leu Leu Val Leu Tyr  
195 200 205

Thr Asp Ser Met Phe Thr Ile Asn Gly Ile Thr Asn Trp Val Gln Gly  
210 215 220

Trp Leu Leu Asn Gly Trp Leu Thr Ser Ala Gly Leu Glu Val Ile Asn  
225 230 235 240

Leu Glu Asp Phe Val Ala Leu Glu Arg Leu Thr Gln Gly Met Asp Ile  
245 250 255

Gln Trp Met His Val Pro Gly His Ser Gly Phe Ile Gly Asn Glu Glu  
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Ala Asp Arg Leu Ala Arg Glu Gly Ala Leu Gln Ser Glu Asp  
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Pro	Cys	Arg	Arg	Gly	Ser	Arg	Gly	Phe	Gly	Met	Phe	Tyr	Ala	Val	Arg	20	25	30	
Arg	Gly	Arg	Leu	Thr	Gly	Val	Phe	Leu	Thr	Trp	Asn	Glu	Cys	Arg	Ala	35	40	45	
Gln	Val	Asp	Arg	Phe	Pro	Ala	Ala	Arg	Phe	Leu	Leu	Phe	Ala	Thr	Glu	50	55	60	
Asp	Glu	Ala	Trp	Ala	Phe	Val	Arg	Leu	Ser	Ala	Ser	Pro	Glu	Val	Ser	65	70	75	80
Glu	Gly	His	Glu	Asn	Gln	His	Gly	Gln	Glu	Ser	Glu	Ala	Leu	Ala	Ser	85	90	95	
Leu	Arg	Leu	Arg	Glu	Pro	Leu	Asp	Gly	Asp	Gly	His	Glu	Ser	Ala	Glu	100	105	110	
Pro	Tyr	Ala	Leu	His	Met	Leu	Pro	Ser	Val	Glu	Pro	Ala	Pro	Pro	Val	115	120	125	
Ser	Arg	Asp	Thr	Phe	Ser	Tyr	Met	Gly	Asp	Phe	Val	Val	Val	Tyr	Thr	130	135	140	
Asp	Gly	Cys	Cys	Ser	Ser	Asn	Gly	Arg	Arg	Arg	Pro	Arg	Ala	Gly	Ile	145	150	155	160
Gly	Val	Tyr	Trp	Gly	Pro	Gly	His	Pro	Leu	Asn	Val	Gly	Ile	Arg	Leu	165	170	175	
Pro	Gly	Arg	Gln	Thr	Asn	Gln	Arg	Ala	Glu	Ile	His	Ala	Ala	Cys	Leu	180	185	190	
Ala	Ile	Glu	Gln	Ala	Leu	Thr	Gln	Asn	Ile	Asn	Leu	Leu	Val	Leu	Tyr	195	200	205	
Thr	Asp	Ser	Met	Phe	Thr	Ile	Asn	Gly	Ile	Thr	Asn	Trp	Val	Gln	Gly	210	215	220	
Trp	Leu	Leu	Asn	Gly	Trp	Leu	Thr	Ser	Ala	Gly	Leu	Glu	Val	Ile	Asn	225	230	235	240
Leu	Glu	Asp	Phe	Val	Ala	Leu	Glu	Arg	Leu	Thr	Gln	Gly	Met	Asp	Ile				

245

250

255

Gln Trp Met His Val Pro Gly His Ser Gly Phe Ile Gly Asn Glu Glu  
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 275 280 285

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<400> 9

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 20 25 30

Arg Gly Arg Leu Thr Gly Val Phe Leu Thr Trp Asn Glu Cys Arg Ala  
 35 40 45

Gln Val Asp Arg Phe Pro Ala Ala Arg Phe Leu Leu Phe Ala Thr Glu  
 50 55 60

Asp Glu Ala Trp Ala Phe Val Arg Leu Ser Ala Ser Pro Glu Val Ser  
 65 70 75 80

Glu Gly His Glu Asn Gln His Gly Arg Glu Ser Glu Ala Leu Ala Ser  
 85 90 95

Leu Arg Leu Arg Glu Pro Leu Asp Gly Asp Gly His Glu Ser Ala Glu  
 100 105 110

Pro Tyr Ala Leu His Met Leu Pro Ser Val Glu Pro Ala Pro Pro Val  
 115 120 125

Ser Arg Asp Thr Phe Ser Tyr Met Gly Asp Phe Val Val Val Tyr Thr  
 130 135 140

Asp Gly Cys Cys Ser Ser Asn Gly Arg Arg Arg Pro Arg Ala Gly Ile  
 145 150 155 160

Gly Val Tyr Trp Gly Pro Gly His Pro Leu Asn Val Gly Ile Arg Leu  
 165 170 175

Pro Gly Arg Gln Thr Asn Gln Arg Ala Glu Ile His Ala Ala Cys Leu  
                   180                  185                  190

Ala Ile Glu Gln Ala Leu Thr Gln Asn Ile Asn Leu Leu Val Leu Tyr  
           195                  200                  205

Thr Asp Ser Met Phe Thr Ile Asn Gly Ile Thr Asn Trp Val Arg Gly  
       210                  215                  220

Trp Leu Leu Asn Gly Trp Leu Thr Ser Ala Gly Leu Glu Val Ile Asn  
   225                  230                  235                  240

Leu Glu Asp Phe Val Ala Leu Glu Arg Leu Thr Gln Gly Met Asp Ile  
                   245                  250                  255

Gln Trp Met His Val Pro Gly His Ser Gly Phe Ile Gly Asn Glu Glu  
                   260                  265                  270

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<213> Homo sapiens

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           20                  25                  30

Val Asp Glu Ala Gly Arg Gly Pro Val Leu Gly Pro Met Val Tyr Ala  
       35                  40                  45

Ile Cys Tyr Cys Pro Leu Pro Arg Leu Ala Asp Leu Glu Ala Leu Leu  
   50                  55                  60

Val Ala Asp Ser Leu Thr Leu Leu Glu Ser Glu Arg Glu Arg Leu Phe  
   65                  70                  75                  80

Ala Leu Met Glu Asp Thr Asp Phe Val Gly Trp Ala Leu Asp Val Leu  
           85                  90                  95

Ser Pro Asn Leu Ile Ser Thr Ser Met Leu Gly Arg Val Leu Tyr Asn

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Leu Asp Gln Gly Val Asn Val 130	Thr Gln Val Phe Val Asp Thr Val Gly 135 140	
Met Pro Glu Thr Tyr Gln Ala Gln Leu Gln Gln Ser Phe Pro Gly Ile 145 150 155 160		
Glu Val Thr Val Leu Ala Leu Ala Asp Ala Leu Tyr Pro Val Val Ser 165 170 175		
Ala Ala Ser Ile Cys Ala Leu Val Ala Arg Asp Gln Ala Val Leu Leu 180 185 190		
Trp Gln Phe Val Glu Leu Leu Gln Asp Leu Asp Thr Asp Tyr Gly Ser 195 200 205		
Gly Tyr Pro Asn Asp Pro Leu Thr Leu Ala Trp Leu Leu Glu His Val 210 215 220		
Glu Pro Val Phe Gly Phe Pro Gln Phe Val Arg Phe Ser Trp Arg Thr 225 230 235 240		
Ala Gln Thr Ile Leu Glu Leu Glu Ala Glu Asp Val Ile Trp Glu Asp 245 250 255		
Ser Ala Ser Glu Asn Gln Glu Gly Leu Arg Leu Ile Thr Ser Tyr Phe 260 265 270		
Leu Asn Glu Gly Ser Gln Ala Arg Pro Arg Ser Ser His Arg Tyr Phe 275 280 285		
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                     20                    25                    30

Arg Gly Arg Arg Thr Gly Val Phe Leu Ser Trp Ser Glu Cys Leu Ala  
                     35                    40                    45

Gln Val Asp Arg Phe Pro Ala Ala Arg Phe Leu Leu Phe Ala Thr Glu  
                     50                    55                    60

Asp Glu Ala Trp Ala Phe Val Arg Ser Ser Ser Ser Pro Asp Gly Ser  
                     65                    70                    75                    80

Leu Gly Gln Glu Ser Ala His Glu Gln Leu Ser Gln Ala Leu Thr Ser  
                     85                    90                    95

Leu Arg Pro Arg Glu Pro Leu Gly Glu Gly Glu Glu Leu Pro Glu Pro  
                     100                    105                    110

Gly Pro Leu His Thr Arg Gln Asp Thr Glu Pro Ala Ala Val Val Ser  
                     115                    120                    125

Leu Asp Thr Phe Ser Tyr Met Gly Glu Ser Val Ile Val Tyr Thr Asp  
                     130                    135                    140

Gly Cys Cys Ser Ser Asn Gly Arg Leu Arg Ala Arg Ala Gly Ile Gly  
                     145                    150                    155                    160

Val Tyr Trp Gly Pro Gly His Pro Leu Asn Val Gly Ile Arg Leu Pro  
                     165                    170                    175

Gly Arg Gln Thr Asn Gln Arg Ala Glu Ile His Ala Ala Cys Leu Ala  
                     180                    185                    190

Ile Met Gln Ala Leu Ala Gln Asn Ile Ser Leu Leu Val Leu Tyr Thr  
                     195                    200                    205

Asp Ser Met Phe Thr Ile Asn Gly Ile Thr Asn Trp Val Gln Gly Trp  
                     210                    215                    220

Leu Leu Asn Gly Trp Arg Thr Ser Thr Gly Leu Asp Val Ile Asn Leu  
                     225                    230                    235                    240

Glu Asp Phe Met Glu Leu Asp Glu Leu Thr Gln Gly Met Asp Ile Gln  
                     245                    250                    255

Trp Met His Ile Pro Gly His Ser Gly Phe Val Gly Asn Glu Glu Ala  
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Asp Arg Leu Ala Arg Glu Gly Ala Leu Gln Ser Glu Asp  
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<211> 1131

<212> DNA

<213> Homo sapiens

<400> 12

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